Pharming Group N.V.
Guggenheim - Genomics Medicine and Rare Disease Days

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Stephen Toor – Chief Commercial Officer

CONFERENCE CALL PARTICIPANTS
Debjit Chattopadhyay – Guggenheim

Debjit Chattopadhyay – Guggenheim:
Well, good afternoon and thank you for joining Guggenheim's Fifth Genomic Medicines and Rare Disease Conference. My pleasure to host the Chief Executive Officer of Pharming, Sijmen de Vries and Chief Commercial Officer, Stephen Toor. First of all, before we get started, congrats on the approval.

Sijmen de Vries, MD – Chief Executive Officer:
Thank you.

Debjit Chattopadhyay – Guggenheim:
Very few companies have two drugs on the market. You guys have two drugs on the market. But before we get to that, given your European roots, a brief introduction to the company would be great.

Sijmen de Vries, MD – Chief Executive Officer:
Yeah, yeah, sure. Thank you. So, we started off as a company that has its own technology platform, Transgenic Animals that was invented by Pharming back in the 1990s. And the resulting product from that, RUCONEST®, our recombinant human C1 esterase inhibitor has been approved for use in hereditary angioedema, acute attacks in both Europe and in the U.S., in Europe since 2010, in the U.S. since 2014. And as many of the European companies, we were having a hard time continuing to attract funding and so on. So, we had to analyze our compound back in the days.

And the whole thing turned around for us when we were able to buy back the North American rights for RUCONEST® back in, let's say end of 2016. And we started commercializing ourselves in North America here for RUCONEST® because hereditary angioedema, that's where the market is in the United States. And we hired Stephen and his team, we got the product back from Valiant, which was the last owner at that point in time.

And we started basically and became overnight a profitable company. That changed the whole scene, of course. Then, of course, when you become a profitable company and you start commercializing, every investor asks, "What's next?" And yet, of course, when you have focused the company to survive, there's very little we had to show for it in the pipeline except some early opportunities.

And we started looking out fairly quickly already to actually add other rare disease assets to our pipeline. Because we pretty quickly discovered that to commercialize in the United States, especially in rare diseases, you need an infrastructure that, not only has a customer facing folks, but also a lot of other people in the company that are highly specialized in making sure that you

get reimbursement, that your patients are taken care of, and that administrative hurdles are helped to be cleared that those patients are facing.

So, in other words, we discovered that it would be relatively straightforward to add another compound to this. And we didn't even have to look for synergies in the market in that respect. Then we came across this product from Novartis back in 2019, leniolisib, which we call now Joenja®, that was actually available for out licensing. We did have to compete against nine other companies who wanted to have this compound from Novartis.

And we were lucky to be the one that actually got it. And we retrospectively learned from Novartis that it was not the $20 million upfront payment that we did because everybody else had bid for a decent upfront as well, but there were some other aspects. And one of the main things that convinced Novartis is that we had proven to be able to commercialize in the U.S. in rare disease space. And that actually was the defining argument I learned later on from Novartis. And we subsequently took the compound on, of course, it was already in the pivotal trial that Novartis had designed together with the FDA.

And, of course, last year, in the beginning of last year, we concluded the pivotal trial that Novartis was conducting and we were supporting and we concluded the trial positively. And from then on, of course, it was all hands on deck to actually make sure that the CMC was in order, of course, because we had a tech transfer from Novartis and to basically have the regulatory filings in order. And yes, we filed with the FDA back at the end of last year.

We got a priority with you from the FDA and of course, I'm very happy that the FDA even concluded the priority review in a positive way four or five days ahead of time, which was very nice surprise, of course, on the Friday when it happened. And that is where basically, our journey comes from. At the same time, we also are unique in that respect that we also commercialized because we also bought back the rights for RUCONEST®® from our partner Sobi in Europe, subsequently.

So, we also have a commercial infrastructure in Europe in place that we actually increased under Stephen's guidance as well to a commercial infrastructure that can now very well handle additional rare disease assets. And of course, Joenja®, I still have to get used to the brand name of course. Joenja® is going to be the first product that will be commercialized with Stephen's team in Europe. And we look towards the Middle East and North African countries where we can commercialize on name patient basis.

And last but not least, Joenja® has enabled us as well to a branch out to Japan into the near future because the Japanese authorities, we have reached agreement on a very straightforward small clinical trial that we have to do in order to be able to hand in and file for Japan. So, we're looking at a company that has now evolved from a one product company in one geography, basically hereditary angioedema in the U.S. into a multiple product company now in the U.S. already, but soon also in Europe.

And of course, planning to get this footprint in Japan as well. And that puts us in a relatively unique position I would say, not only for a European company, but also for a US company that is still a relatively small company. We employ about 400 people on both sides of the ocean. So that was sort of quick introduction.

Debjit Chattopadhyay – Guggenheim:
That was awesome. So, on Joenja®, can we talk about first the pricing and the labels that you just

got, and then let's talk about boots on the ground, et cetera, to lead the commercial effort.

Sijmen de Vries, MD – Chief Executive Officer:
Okay. Sure, go ahead.

Stephen Toor – Chief Commercial Officer:
Okay. So, in terms of pricing, we have published the price of 547,500 per year. To back out of that headline, we did exude expect extensive research with government payers, commercial payers covering about 112 million patient lives. And we also tip the analogs as well of other small molecules and other rare diseases with similar severity profiles. And what we concluded is this is in that mid-range, it's benchmarks well to other ultra-rare disease pricing, but the things I would add is this is obviously a progressive disease, it's a severe disease, and Joenja® itself, it's a precision medicine.

If you do the genetic test and you test positive for APDS one or two, then a physician knows they're using the right treatment because there is no other indicated treatment that treats the underlying cause and the payer knows they're paying for the right medicine. Now in terms of commercialization itself, we've actually had, typically launch preparation is anywhere from 6 to 12 months as an average. We've had almost three years to prepare for this launch. So, it's the best prepared launch it's ever been my pleasure to help lead. And in terms of the go, so we've had the time to identify patients, we think there are at least 1,500 globally, we have 500 now globally and approximately half of those are in the U.S. and that includes a couple of dozen that are in the open label extension of the expanded access program.

So, they'll come online slightly earlier. The identification part of it, so I think the secret to success for commercializing of these types of products are find, treat, keep or find patients, treat patients, keep patients, especially when there's obviously so few of them, they're in so much need. So, our effort as pre-launch was all around identification and education, so making sure people understood the constellation of symptoms so that when they saw enlargement of organs, bronchiectasis, recurrent infections, et cetera, they would immediately think, okay, test for APDS. So that's how we went about that.

The second part to that, I guess is not being complacent around differentiating. So, every product that they're currently using and current treatments can run into the hundreds of thousands of dollars a year, don't actually work, they don't treat the underlying cause of the disease. And then the fourth part of that is access. So now that we have launched, just having a very robust patient services division, and a hub, and a single point pharmacy that are specifically dedicated to APDS with clinical pharmacists that are dedicated to APDS, so that when a patient is prescribed the product, they can access that as quickly as possible and get on paid therapy.

Debjit Chattopadhyay – Guggenheim:
Got it. And how many patients do you have currently on the AP who could roll over to the commercial side?

Stephen Toor – Chief Commercial Officer:
We have a couple of dozen on the OLE and the AP. I would expect the AP to convert a little bit quicker than the OLE because that involves NIH and is more spread. So, I would think from both groups in the next few months we should expect to see those convert over.

Debjit Chattopadhyay – Guggenheim:

Got it.

Stephen Toor – Chief Commercial Officer:

And we also have obviously, a bank of those roughly 200 plus patients I mentioned, for the most part we know the position, we know the institution, we know where they are. It's just a question of now that we have a label, we can talk directly about Joenja®, the brand, just talking about the product X features, why it's important, and then getting the position and the patient comfortable with moving forward.

Debjit Chattopadhyay – Guggenheim:

And when you talk about find, treat, keep, you have data suggesting these patients once on trial can go up 3, 4, 5 years based on the data you already have?

Stephen Toor – Chief Commercial Officer:

In theory, I mean they could be on the product for life depending on the evolution of the disease because right now, we don't have super long-term data, but we have data anywhere between two and seven years and all of those patients for the most part have done very well.

Debjit Chattopadhyay – Guggenheim:

So on a lifetime revenue per patient perspective, this is going to be pretty significant at whatever 563,000?

Stephen Toor – Chief Commercial Officer:

Absolutely, yeah.

Debjit Chattopadhyay – Guggenheim:

Got it. And how many boots on the ground do you have currently-

Stephen Toor – Chief Commercial Officer

Just so in-

Debjit Chattopadhyay – Guggenheim:

... dedicated to Joenja®?

Stephen Toor – Chief Commercial Officer

So dedicated specifically to Joenja® is 27. So that's at the higher end of a rare disease sales force and that's 24 sales representatives and three sales leaders, all of them come from rare disease, new launch, and patient funded background. So, we've very specifically chosen people who are used to doing the type of job that basically, we're asking them to do. They're focused mainly on the institution. So, there's approximately 400 various types of hospitals, institutions, JMF foundations, where most rare disease patients in the country will flow through eventually once people start to recognize there's something going on here that their pediatrician or their internal med is not going to be able to handle.

Secondarily to that though, we have another team of 27, again 24 sales reps and three leaders, who are actually the RUCONEST® team. So that's already a team that have more than proven themselves in turning that product around and turning into a $200 million plus brand. And we think given that

a lot of those allergy or immunologists or combo that about 30% of the patients will sit there. So between those two sales forces, in total probably larger than you would typically expect, we think we have the majority of the market covered and it also enables us to, one would hope, accelerate progress.

Debjit Chattopadhyay – Guggenheim:
Got it. So, you address the key part of the equation from a durability perspective, how difficult is it to find the patients?

Stephen Toor – Chief Commercial Officer
It's not easy because obviously, there's relatively few of them, but I would say it's really a combination of understanding really, in quite a lot of depth the patient journey, and we've had a lot of time to work that out. We've been working with the steering committee of physicians who have pretty much been treating most of the treated patients or the patients that are in the NIH trial have gone through one of these 10 or 12 KOLs. So, we understood the patient journey very well, good analytics which have evolved over time, partnering with organizations like the JMF, the AKI, Quad AI, the IDF. And I think putting that together, you end up with a pretty good understanding of where patients will sit it and where to go to find them. So, it's not super easy, but it's a relatively well-trodden path, which is how we've got pretty quick progress from a standing start less than two years ago to 500 identified today.

Sijmen de Vries, MD – Chief Executive Officer:
An interesting thing is that we were at ASH last year in December, because that's where our long-term safety data, long-term extension trial data was presented by the principal investigator, and we had a small stand there hidden in plain sight. I think that's exactly the theme, and it reverberated very well with the hematologist because they're treating, let's say lymphoma patients, which is of course unfortunately, happening in a very significant percentage of patients in their late teens, early twenties. And basically the question like, okay, if you see a young patient like that with lymphoma, maybe there's an underlying disease, maybe there is an inborn error of their immune system.

That really is a message that reverberated very well. We got a lot of leads out of that of course, as well because that got them thinking basically. And the same thing applies to where we go to at Quad AI and we have the same theme. We need to do a lot of disease awareness and a lot of education in that respect with those specific treater groups that actually can treat these patients, it can be the immunologist, the hematologist, it can be the pulmonologist, it can also be the gastroenterologist because arthropathy is also a big issue with these patients. So yes, we have a lot of legwork to do, but as Stephen alluded, we have quite a few people there that are actually specialized in this and are very experienced and we are very confident that we can find a significant number of those patients.

And the other thing is, of course, if there is no treatment for a disease, yes you know can test and it's part of the standard immunology panel, this test for APDS, then there's not too much reward for testing. That's why we believe also that ... and that's always been, of course, the case. Now there is a precision medicine available that is actually disease modifying. It will motivate people a lot more to be a little bit more curious about what's going on and tests. So, we are quite optimistic about this whole thing, both of those elements.

Stephen Toor – Chief Commercial Officer:
One thing to add because it's the right question, which is how easy it will be to be defined, it's worth

to remember as well that the disease is autosomal dominant. So, when you find one patient, then family mapping and family testing becomes, I think, fairly critical because the disease has full penetrant, so there will probably be other family members with it even if they're not showing symptoms. And eventually those symptoms, unfortunately, will progress and evolve and they'll start to suffer as well. So that will be a big part of what we do moving forward.

Debjit Chattopadhyay – Guggenheim:
And what's the average age of diagnosis currently?

Stephen Toor – Chief Commercial Officer:
I'm not sure on a specific, but I know there are patients who've been diagnosed as early as one or two years old.

Debjit Chattopadhyay – Guggenheim:
And how big was the phase three study, 30 some patients or something?

Stephen Toor – Chief Commercial Officer:
31.

Debjit Chattopadhyay – Guggenheim:
How quickly did that enroll? Because that indirectly gives you a sense of-

Sijmen de Vries, MD – Chief Executive Officer:
Well yes and no of course, because Novartis run that study and as you can imagine that was not one of Novartis's priority studies so that took a long time. That's why we have exposure up to seven years. Once we started working on it was COVID, so it was also not very helpful. But on the other hand, we were very much encouraged of course, that following the end result of the studies and during the study running, when we started looking for those patients, we were already able to discover there's more than 500 patients. That's the other interesting bit is that we've already found patients to the extent that there's at least one in a million that's already been identified.

We found, for instance, an informal registry in France where there's already 60 patients in the registry, which means that there's a confirmation here that there is at least one in a million in the population available. There's no reason why that, if that's the case in France, why they should not be in the U.S. And like Stephen says, we're also well on our way already to do one in a million in the U.S. Because that's the name of the game room, as we know, in all the rare diseases, companies tout a lot of wonderful numbers ahead of commercialization, but having those patients really in your database, that's another matter here and that's what we have to a great extent already.

Debjit Chattopadhyay – Guggenheim:
And in terms of motivation for these patients to get on therapy or physician interest I can see, but what's the market research feedback that you have?

Sijmen de Vries, MD – Chief Executive Officer:
It's really life changing. These patients can't do anything. There are all sorts of physical elements that they suffer from, it's mental issues that they have, there is social issues that they can't do anything, they cannot work, they can't go to school and they're spending their lives in hospital. So, it's really a very miserable disease with an ongoing downward spiral. Despite all the interventions,

despite all the treatments, despite the regular immunoglobulin injections that they have to undergo, there's really no way that it goes upwards, it goes all the way downwards the spiral. When you look at our clinical trial population, the majority of the clinical trial population is younger than 20 years. The label is from 12 years and upwards of course, now, so it's between 12 and upwards. There's a lot of these young patients in there. So, it's a very, very debilitating disease.

And the good news is you see already in that 12-week trial, you see already a significant improvement in all these parameters and in the patient. If you read the patient narratives, it is very motivating to see that already in that 12-week trial, they start feeling different, they start seeing all sorts of the symptoms disappear. And if you look at the long-term extension data, that's even more wonderful because you really see that continuously over time, they have a tendency to improve further. And that's why everybody stays on that product. There's nobody that I know of has dropped out of that long-term extension study, except one older person who died for unrelated courses. So it's really a wonderful result in that respect, and a great testament to this compound. And I know that PI3 kinase delta inhibitors may not have a very good reputation, but this one seems to be doing the trick.

We have a double-blind placebo control trial with a side effect profile that's equal to placebo to start with. And then we have basically confirmed in that long-term extension tail of about two to 7 up to 7 years, only average two years where basically the tolerability is basically similar to that, what you get reported in the open label trial. So that's why we think that these patients will be very motivated, given the ones that are in the clinical trial that are very motivated to continue. We believe that the patients that will go on drug will be very motivated to do this because this is really good results.

And even more, because between the dose find that Novartis did in the first six patients, there was a time in between when they could not have access to the drug and that's actually for various reasons, administrative reasons, but also sometimes COVID reasons. And you see immediately the parameters in this case was the IGM, it goes down very nicely during the dose finding study. They stop, it goes immediately up, and then when they start treating the open label, they're taking the open label medication, it goes very rapidly down again. So, it's really a school example, I would say, of how you want patients to respond to the drug.

Debjit Chattopadhyay – Guggenheim:
So, the current label is 12 and older. What do you have to do to get the 2 to 12 given some patients going to be diagnosed at two? And in Japan, the study that you're conducting to get approved, would that enroll two and older?

Stephen Toor – Chief Commercial Officer:
So, we are running two pediatric trials, 4 through 11 has started. And we have our first patient in and I think, the one to four will start using granules, so that's not the tablets, I'll say second half of this year, I think later this year.

Sijmen de Vries, MD – Chief Executive Officer:
Yeah.

Stephen Toor – Chief Commercial Officer:
The Japanese trial is three patients and I believe that's 12 and older as well. So that will give us our bridgehead into the Japanese market, which will, I believe, probably commercialize ourselves rather than partner out because this is a very manageable size of disease. So, I would hope by mid '25 as

a rough estimate that we would be launching the pediatric conjugation in the U.S. and then slightly later probably in Europe.

Debjit Chattopadhyay – Guggenheim:
Got it. And a month or so ago, Europe or maybe a few weeks ago, Europe pushed it to a standard review. What triggered that?

Sijmen de Vries, MD – Chief Executive Officer:
Yeah, the reason was that whereas the FDA, we submitted the same file to the FDA and IMA and that file included the long-term extension data up to the end of '21 I believe, yes, up to the end of 21. That was sufficient for the FDA, that was what we just described and what was actually published and what actually presented at ASH what I just quoted from. And the Europeans then came back and basically told us that they know the study continues to go on and they would like to have another data cutoff point later on in time. Now, when you are on the accelerated review with the Europeans, if you don't answer their list of questions within 30 days, you're basically automatically out.

And if you get a question like that, you're back to the normal schedule by the way, sorry, allowed you back to the normal schedule. And when you get a question about an analysis like that, the data is already there but the analysis is not done, of course. You can't do that within 30 days. That was the reason why they said, "Okay, we'll reset you to the normal schedule." And that's where we are all now and that is why we submit that data that's already in our hands, but needs to be analyzed, and needs to be put in the right format, and then basically speaking, it moves on. So we're very confident that the European authorities will also probably, come back with a positive verdict later on this year, the second half.

Debjit Chattopadhyay – Guggenheim:
Given that it's a PI3 K Delta, there could be a myriad of other applications for this.

Sijmen de Vries, MD – Chief Executive Officer:

Yeah.

Debjit Chattopadhyay – Guggenheim:
Where are you thinking of taking this given that you're technically a profitable company?

Sijmen de Vries, MD – Chief Executive Officer:
Yeah, well when you take a compound from Novartis, the other bit of good news is that they've done some significant research collaborations already on additional indications. So, I would say we have few indications that we looked at and we are at the moment prioritizing ourselves into the where we think the best thing next to go would be. And that is actually under review, we haven't disclosed anything like that yet. But there's a lot of related immune deficiencies here that where PI3 Kinase Delta pathway plays an important role. So, we will, of course, update the market more precisely on the indications later on this year, but we haven't made up our mind fully yet where to go. But we have a few things on the review here internally, and like I said, in the second half of this year we will be able to disclose this to the market where we go.

Stephen Toor – Chief Commercial Officer:
I think that's actually, that you mentioned earlier, so that's the exciting part. We have RUCONEST®,

which is turned around in the U.S. and is doing very well. We have Joenja® just launching with what, I think for me in my career, is the best plan launch I've been associated with. And we have this opportunity to build a franchise around leniolisib, and that's before we talk about any business development opportunities or any other development activities that we might do outside of there. So this is really a significant inflection point for us as a company.

Debjit Chattopadhyay – Guggenheim:
And for your HAE product, one concern that people do have seems to be the IP, but based on your conviction, there is no way of trying to make a copycat or biosimilar product.

Sijmen de Vries, MD – Chief Executive Officer:
We can be very simple about it. It is a transgenic animal platform, so we think that's a very high hurdle for entry because expressing C1 inhibitor in a way that is non immunogenic has proven to be very difficult. RUCONEST® has clearly proven over time to be non-immunogenic. We have, what 150,000 plus treatments under our belts and counting. People have used it hundreds of times, individual patients, we see no sign of any in immunogenicity, which in itself for a biological is quite unique I would say.

So therefore, we believe that the exclusivity, the regulatory exclusivity which will expire in this country in '26 and the Europe in '25 will mean nothing, basically speaking, because nobody will be able to be actually bothered as well because it's a relatively modest size product, it's 200 million business to actually go to all this trouble to start a transgenic platform just to make that one compound C1 inhibitor. That's our opinion internally and therefore we think RUCONEST® will have a significant longer commercial tail than everybody is anticipating or what may be anticipating

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Debjit Chattopadhyay – Guggenheim:
Got it. So RUCONEST®, let's say 200 million, Joenja® could be multiples of that if given how sick these patients are.

Sijmen de Vries, MD – Chief Executive Officer:
Yep.

Debjit Chattopadhyay – Guggenheim:
What do you plan to do with the cash flows?

Sijmen de Vries, MD – Chief Executive Officer:
Well, the cash flows we will very happily invest in additional in licensing opportunities/ acquisitions because that is what we are doing as well. We know as a resident outset, we have a very scalable commercial model. We have this commercial infrastructure in place, so it's fairly easy to actually bolt on additional rare disease assets and that's what we are doing. Our small BD group is turning over a lot of opportunities where we look for clinical proof of concept and we're happy to take the pivotal trial risk, but the closer to the market of course, the happier because Stephen and his team wants to have, as soon as possible, other products in the bag. And that's what we're hunting for. So basically to summarize it, we're hunting for additional real serious rare disease assets where we can make the difference and where we can show our capabilities to commercialize, yet again, that we will show with Joenja® as well.

Debjit Chattopadhyay – Guggenheim:
Awesome so sum it up for 2023, what are we looking for?

Sijmen de Vries, MD – Chief Executive Officer:
What are we looking for? We're looking, hopefully, for an additional asset that we could get in-house and of course, we're looking for Stephen and team to start delivering on Joenja® and continuing to actually keep our RUCONEST® business. I think we still guide for a single digit growth this year, so we are really looking forward to this year where we add Joenja® sales, which will begin in earnest very soon in this country to the RUCONEST® business and then hopefully get an asset as well. But the assets, we are very precise about, it needs to be a serious, rare disease. This needs to be a product that makes a serious difference and I think Joenja® is a very good case in point in this respect.

Debjit Chattopadhyay – Guggenheim:
Awesome. I appreciate it so much Sijmen. Thank you for that

Sijmen de Vries, MD – Chief Executive Officer:
Thank you very much, Debjit.

Debjit Chattopadhyay – Guggenheim:
Thanks.

[end of transcript]